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=> s trimer?
L1 53714 TRIMER?

=> s mutant? or mutein? or variant? or wild?
L2 1609354 MUTANT? OR MUTEIN? OR VARIANT? OR WILD?

=> s dominant-negative or dominant (w) negative
L3 46867 DOMINANT-NEGATIVE OR DOMINANT (W) NEGATIVE

=> s l2 (s) l3
L4 23245 L2 (S) L3

=> s l4 (s) l1
L5 52 L4 (S) L1

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L6 ANSWER 1 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2003362578 EMBASE
TITLE: Interactions of FliJ with the Salmonella type III flagellar export apparatus.
AUTHOR: Fraser G.M.; Gonzalez-Pedrajo B.; Tame J.R.H.; Macnab R.M.
CORPORATE SOURCE: R.M. Macnab, Dept. Molec. Biophys./Biochem. 0734, Yale University, 266 Whitney Ave., New Haven, CT 06520-8114, United States. robert.macnab@yale.edu
SOURCE: Journal of Bacteriology, (2003) 185/18 (5546-5554).
Refs: 22
ISSN: 0021-9193 CODEN: JOBAAY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB FliJ, a 17-kDa protein, is a soluble component of the Salmonella type III flagellar protein export system that has antiaggregation properties and several other characteristics that suggest it may have a chaperone-like function. We have now examined this protein in detail. Ten-amino-acid scanning deletions covering the entire 147-amino-acid sequence were tested for complementation of a fliJ null strain; only the first and last deletions complemented. A few of the deletions, especially towards the C terminus, exerted a ***dominant*** ***negative*** effect on ***wild*** -type cells, indicating that they were actively interfering with function. Two truncated versions of FliJ, representing its N- and C-terminal halves, failed to complement and were not dominant. We tested for FliJ self-association by several techniques. Size-exclusion chromatography (Superdex 200) indicated an apparent molecular mass of around 50 kDa, which could reflect either multimerization or an elongated shape or both. Multiangle light scattering gave a peak value of 20 kDa, close to the molecular mass of the monomer. Analytical ultracentrifugation gave evidence for weak self-association as a ***trimer*** or tetramer. It was known from previous studies that FliJ interacts with the N-terminal region of FliH, a negative regulator of the ATPase FliI. Using both truncation and deletion versions of FilJ, we now show that it is its C-terminal region that is responsible for this interaction. We also show that FliJ interacts with the soluble cytoplasmic domain of the largest membrane component of the export apparatus, FlhA; although small deletions in FliJ did not interfere with the association, both truncated versions failed to associate, indicating that a substantial amount of the central

region of the FliJ sequence participates in the association. We present a
model summarizing these multiple interactions.

L6 ANSWER 2 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 1
ACCESSION NUMBER: 2002309005 EMBASE
TITLE: Collagen X chains harboring Schmid metaphyseal
chondrodysplasia NC1 domain mutations are selectively
retained and degraded in stably transfected cells.
AUTHOR: Wilson R.; Freddi S.; Bateman J.F.
CORPORATE SOURCE: J.F. Bateman, Murdoch Childrens Research Institute, Royal
Children's Hospital, Parkville, Vic. 3052, Australia.
bateman@cryptic.rch.unimelb.edu.au
SOURCE: Journal of Biological Chemistry, (12 Apr 2002) 277/15
(12516-12524).
Refs: 35
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Collagen X is a short chain, homotrimeric collagen expressed specifically
by hypertrophic chondrocytes during endochondral bone formation and
growth. Although the exact role of collagen X remains unresolved,
mutations in the COL10A1 gene disrupt growth plate function and result in
Schmid metaphyseal chondrodysplasia (SMCD). With the exception of two
mutations that impair signal peptide cleavage during .alpha.1(X) chain
biosynthesis, SMCD mutations are clustered within the carboxyl-terminal
NC1 domain. The formation of stable NC1 domain ***trimers*** is a
critical stage in collagen X assembly, suggesting that mutations within
this domain may result in subunit mis-folding or reduce ***trimer***
stability. When expressed in transiently transfected cells, .alpha.1(X)
chains containing SMCD mutations were unstable and presumed to be degraded
intracellularly. More recently, in vitro studies have shown that certain
missense mutations may exert a ***dominant*** ***negative***
effect on .alpha.1(X) chain assembly by formation of ***mutant***
homotrimers and normal- ***mutant*** heterotrimers. In contrast,
analysis of cartilage tissue from two SMCD patients revealed that the
truncated ***mutant*** message was fully degraded, resulting in 50%
reduction of functional collagen X within the growth plate. Therefore, in
the absence of data that conclusively demonstrates the full cellular
response to ***mutant*** collagen X chains, the molecular mechanisms
underlying SMCD remain controversial. To address this, we closely examined
the effect of two NC1 domain mutations, one frameshift mutation
(1963del10) and one missense mutation (Y598D), using both
semipermeabilized cell and stable cell transfection expression systems.
Although able to assemble to a limited extent in both systems, we show
that, in intact cells, collagen X chains harboring both SMCD mutations did
not evade quality control mechanisms within the secretory pathway and were
degraded intracellularly. Furthermore, co-expression of ***wild***
-type and ***mutant*** chains in stable transfected cells demonstrated
that, although ***wild*** -type chains were secreted, ***mutant***
chains were largely excluded from hetero-***trimer*** formation. Our
data indicate, therefore, that the predominant effect of the NC1 mutations
Y598D and 1963del10 is a reduction in the amount of functional collagen X
within the growth cartilage extracellular matrix.

L6 ANSWER 3 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 2
ACCESSION NUMBER: 2001045457 EMBASE
TITLE: CD154 variant lacking tumor necrosis factor homologous
domain inhibits cell surface expression of wild-type
protein.
AUTHOR: Su L.; Garber E.A.; Hsu Y.-M.
CORPORATE SOURCE: Y.-M. Hsu, Dept. of Protein Engineering, Biogen, Inc., 12
Cambridge Center, Cambridge, MA 02142, United States.
yen-ming_hsu@biogen.com
SOURCE: Journal of Biological Chemistry, (19 Jan 2001) 276/3
(1673-1676).
Refs: 17
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB X-linked hyper-IgM (XHIM) syndrome is an immunological disorder resulting
from mutations in the CD154 gene. Some mutations occur in splicing sites
and result in transcripts encoding ***wild*** -type and ***mutant***
proteins. These ***mutants*** lack the tumor necrosis factor
homologous (TNFH) domain and consequently fail to ***trimerize*** .
Given that the TNFH domain is responsible for ***trimerization*** , one

may predict that the TNFH ***mutant*** can not participate in the assembly of ***wild*** -type CD154. Thus, it was puzzling why these patients exhibit XHIM pheno-type, presumably resulting from a lack of functional CD154. One possibility is that the TNFH ***mutant*** exhibits a ***dominant*** ***negative*** effect over the ***wild*** -type protein. To investigate this, we coexpressed the ***wild*** -type protein and a TNFH ***mutant*** and examined the biochemical and functional properties of the resulting CD154 products. We demonstrate that despite the lack of the TNFH domain, the TNFH ***mutant*** can associate with the ***wild*** -type protein. Furthermore, such an association compromises the ability of the ***wild*** -type protein to mature onto the cell surface. These results provide a mechanism for the defect of CD154 in XHIM patients producing both ***wild*** -type and TNFH ***variants*** and suggest that besides the TNFH domain, the stalk region participates in the assembly of CD154 ***trimers*** .

L6 ANSWER 4 OF 31 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001267781 MEDLINE
DOCUMENT NUMBER: 21257784 PubMed ID: 11358428
TITLE: Coexpression of normal and mutated CD40 ligand with deletion of a putative RNA lariat branchpoint sequence in X-linked hyper-IgM syndrome.
AUTHOR: Zhu X; Chung I; O'Gorman M R; Scholl P R
CORPORATE SOURCE: Disease Pathogenesis Program, Children's Memorial Institute for Education and Research, Chicago, Illinois 60614, USA.
SOURCE: CLINICAL IMMUNOLOGY, (2001 Jun) 99 (3) 334-9.
Journal code: 100883537. ISSN: 1521-6616.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621
AB We describe a novel CD40 ligand (CD40L) splicing mutation in a patient with X-linked hyper-IgM syndrome (X-HIM) associated with alternate splicing of exon 3, resulting in the expression of both full-length and exon-3-skipped CD40L mRNA. The mutation is an 8-bp deletion 25 bp upstream of the intron 2/exon 3 junction which overlaps a putative RNA branchpoint, suggesting that it may impair RNA lariat formation. The exon-3-skipped CD40L transcript encodes a truncated protein (CD40LDeltaE3) encompassing the cytoplasmic, transmembrane, and extracellular stalk domains, but lacking the CD40L receptor binding domain. CD40LDeltaE3 protein expression was readily detectable in transfected Cos cells by immunofluorescence. In cells cotransfected with CD40LDeltaE3 and ***wild*** -type CD40L, expression of CD40LDeltaE3 did not inhibit the expression of ***wild*** -type CD40L monomers, but strongly inhibited staining by the conformationally sensitive anti-CD40L mAb 5c8, suggesting that CD40LDeltaE3 acts in a ***dominant*** ***negative*** manner to inhibit the assembly of functional CD40L ***trimers*** . This mechanism may contribute to the pathophysiology of CD40L deficiency in X-HIM patients with leaky splice site mutations.

L6 ANSWER 5 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 4
ACCESSION NUMBER: 2001118615 EMBASE
TITLE: Alternative activation of extracellular signal-regulated protein kinases in curcumin and arsenite-induced HSP70 gene expression in human colorectal carcinoma cells.
AUTHOR: Chen Y.-C.; Tsai S.-H.; Shen S.-C.; Lin J.-K.; Lee W.-R.
CORPORATE SOURCE: Prof. Y.-C. Chen, Graduate Institute of Pharmacognosy, Taipei Medical College, 250 Wu-Hsing St., Taipei, Taiwan,Province of China. yc3270@tmc.edu.tw
SOURCE: European Journal of Cell Biology, (2001) 80/3 (213-221).
Refs: 52
ISSN: 0171-9335 CODEN: EJCBDN
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have investigated the regulation mechanism of chemical stress-induced HSP70 gene expression in human colorectal carcinoma cells (COLO205 and HT29). Our data show that chemical treatments including sodium arsenite and curcumin, induced significant synthesis of HSP70 and its mRNA. The induced HSP70 gene expression appears to be increased at the

transcriptional level. The increase in HSP70 gene expression by both
chemicals is associated with an increase in HSF binding to HSE and
induction of HSF1 di- or ***trimerization*** . Phosphorylation and
activation of extracellular signal-regulated proteins (ERK1/2) were
detected in sodium arsenite-treated COLO205 and HT29 cells, and the free
radical scavenger N-acetyl-L-cysteine (NAC) was able to inhibit this
ERK1/2 activation and HSP70 gene expression. MAPK blockade by the specific
MEK1 inhibitor (PD98059) decreased the ability of sodium arsenite to
increase HSP70 gene expression in a dose-dependent manner along with
dephosphorylation of ERK1/2 proteins. In contrast to arsenite treatment,
activation of ERK1/2 was not detected in curcumin-treated colorectal
carcinoma cells, and NAC and PD98059 did not show any inhibitory effect on
HSP70 gene expression induced by curcumin. Overexpression of a
dominant ***negative*** ***mutant*** of mitogen-activated
protein kinase kinase kinase 1 (MEKK1-DN) prevents arsenite-induced ERK1/2
phosphorylation and HSP70 protein synthesis. These results indicated that
the ERK signaling pathway can participate in HSP70 gene expression induced
by the prooxidant sodium arsenite, but not by the antioxidant curcumin.

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on STN DUPLICATE 5
ACCESSION NUMBER: 2001258772 EMBASE
TITLE: Association of phosphatidylinositol 3-kinase composed of
p110.beta.-catalytic and p85-regulatory subunits with the
small GTPase Rab5.
AUTHOR: Kurosu H.; Katada T.
CORPORATE SOURCE: T. Katada, Dept. of Physiological Chemistry, Grad. Sch. of
Pharmaceut. Sciences, University of Tokyo, 7-3-1 Hongo,
Bunkyo-ku, Tokyo 113-0033, Japan. katada@mol.f.u-
tokyo.ac.jp
SOURCE: Journal of Biochemistry, (2001) 130/1 (73-78).
Refs: 31
ISSN: 0021-924X CODEN: JOBIAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A family of phosphatidylinositol 3-kinases (PI 3-kinase), comprising three
major classes (I-III) in terms of substrate specificity and regulation,
play important roles in a variety of cell functions. We previously
reported that the class-I heterodimeric PI 3-kinase consisting of
p110.beta.-catalytic and p85-regulatory subunits is synergistically
activated by two different types of membrane receptors, one possessing
tyrosine kinase activity and the other activating ***trimeric*** G
proteins. Here we report an additional unique feature of the
p110.beta./p85 PI 3-kinase. The small GTPase Rab5 was identified as a
binding protein for the p110.beta.-catalytic subunit in a yeast two-hybrid
screening system. The interaction appears to require at least two
separated amino-acid sequences present specifically in the .beta. isoform
of p110 and the GTP-bound form of Rab5. The expressions of constitutively
active and ***dominant*** ***negative*** ***mutants*** of Rab5
in THP-1 cells induce the stimulation and inhibition, respectively, of
protein kinase B activity, which is dependent on the PI 3-kinase product
phosphatidylinositol 3,4,5-triphosphate. These results suggest that there
is a specific interaction between GTP-bound Rab5 and the p110.beta./p85 PI
3-kinase, leading to efficient coupling of the lipid kinase product to its
downstream target, protein kinase B.

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on STN DUPLICATE 6
ACCESSION NUMBER: 2001259607 EMBASE
TITLE: Analysis of dominant-negative effects of mutant Env
proteins of human immunodeficiency virus type 1.
AUTHOR: Iwatani Y.; Kawano K.; Ueno T.; Tanaka M.; Ishimoto A.; Ito
M.; Sakai H.
CORPORATE SOURCE: H. Sakai, Department of Viral Oncology, Institute for Virus
Research, Kyoto University, Sakyo-Ku, Kyoto 606-8507,
Japan. hsakai@virus.Kyoto-u.ac.jp
SOURCE: Virology, (20 Jul 2001) 286/1 (45-53).
Refs: 44
ISSN: 0042-6822 CODEN: VIRLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The Env protein of human immunodeficiency virus type 1 is assembled into a
stable ***trimer*** , and oligomerization is required for maintenance
of viral infectivity. This property of Env suggests that Env
mutants may have a ***dominant*** -***negative*** effect on
virus infectivity. To investigate this possibility, we established a
packaging cell line in which both ***wild*** -type and ***mutant***

Env proteins could be expressed simultaneously in a single cell. We
analyzed the effects of two types of Env ***mutants*** : cytoplasmic
tail-truncated TM ***mutants*** and a ***mutant*** defective in
gp120/gp41 cleavage. The cytoplasmic tail-truncated proteins were found to
be incorporated into virions by forming an oligomer with ***wild***
-type TM, but could not inhibit the ***wild*** -type function. In
contrast, phenotypic mixing of cleavage-defective Env with the
wild -type protein caused dramatic inhibition of infectivity,
indicating that this ***mutant*** has a strong ***dominant*** -
negative phenotype. .COPYRGT. 2001 Academic Press.

L6 ANSWER 8 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2001006370 EMBASE
TITLE: Binding of BiP to the processing enzyme lymphoma proprotein
convertase prevents aggregation, but slows down maturation.
AUTHOR: Creemers J.W.M.; Van de Loo J.-W.H.P.; Plets E.; Hendershot
L.M.; Van de Ven W.J.M.
CORPORATE SOURCE: Dr. J.W.M. Creemers, Laboratory for Molecular Oncology,
Center for Human Genetics, University of Leuvin, Herestraat
49, 3000 Leuven, Belgium. john.creemers@med.kuleuven.ac.be
SOURCE: Journal of Biological Chemistry, (8 Dec 2000) 275/49
(38842-38847).
Refs: 55
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Lymphoma proprotein convertase (LPC) is a subtilisin-like serine protease
of the mammalian proprotein convertase family. It is synthesized as an
inactive precursor protein, and propeptide cleavage occurs via
intramolecular cleavage in the endoplasmic reticulum. In contrast to other
convertases like furin and proprotein convertase-1, propeptide cleavage
occurs slowly. Also, both a glycosylated and an unglycosylated precursor
are detected. Here we demonstrate thai the unglycosylated precursor form
of LPC is localized in the cytosol due to the absence of a signal peptide.
Using a reducible cross-linker, we found that glycosylated pro-LPC is
associated with the molecular chaperone BiP. In addition, we show that
pro-LPC is prone to aggregation and forms large complexes linked via
interchain disulfide bonds. BiP is associated mainly with non-aggregated
pro-LPC and pro-LPC dimers and ***trimers*** , suggesting that BiP
prevents aggregation. Overexpression of ***wild*** -type BiP or a
dominant - ***negative*** BiP ATPase ***mutant*** resulted
in reduced processing of pro-LPC. Taken together, these results suggest
that binding of BiP to pro-LPC prevents aggregation, but results in slower
maturation.

L6 ANSWER 9 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2000332799 EMBASE
TITLE: Reconstitution of the KRAB-KAP-1 repressor complex: A model
system for defining the molecular anatomy of RING-B
box-coiled-coil domain-mediated protein-protein
interactions.
AUTHOR: Peng H.; Begg G.E.; Schultz D.C.; Friedman J.R.; Jensen
D.E.; Speicher D.W.; Rauscher III F.J.
CORPORATE SOURCE: F.J. Rauscher III, Wistar Institute, 3601 Spruce Street,
Philadelphia, PA 19104, United States.
rauscher@wista.wistar.upenn.edu
SOURCE: Journal of Molecular Biology, (4 Feb 2000) 295/5
(1139-1162).
Refs: 61
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The KRAB domain is a 75 amino acid residue transcriptional repression
module commonly found in eukaryotic zinc-finger proteins. KRAB-mediated
gene silencing requires binding to the corepressor KAP-1. The KRAB:KAP-1
interaction requires the RING-B box-coiled coil (RBCC) domain of KAP-1,
which is a widely distributed motif, hypothesized to be a protein-protein
interface. Little is known about RBCC-mediated ligand binding and the role
of the individual sub-domains in recognition and specificity. We have
addressed these issues by reconstituting and characterizing the
KRAB:KAP-1-RBCC interaction using purified components. Our results show
that KRAB binding to KAP-1 is direct and specific, as the related RBCC
domains from TIF1.alpha. and MID1 do not bind the KRAB domain. A
combination of gel filtration, analytical ultracentrifugation, chemical
cross-linking, non-denaturing gel electrophoresis, and site-directed

mutagenesis techniques has revealed that the KAP-1-RBCC must oligomerize
likely as a homo- ***trimer*** in order to bind the KRAB domain. The
RING finger, B2 box, and coiled-coil region are required for
oligomerization of KAP-1-RBCC and KRAB binding, as mutations in these
domains concomitantly abolished these functions. KRAB domain binding
stabilized the homo-oligomeric state of the KAP-1-RBCC as detected by
chemical cross-linking and velocity sedimentation studies. ***Mutant***
KAP-1-RBCC molecules hetero-oligomerize with the ***wild*** -type
KAP-1, but these complexes were inactive for KRAB binding, suggesting a
potential ***dominant*** ***negative*** activity. Substitution of
the coiled-coil region with heterologous dimerization, ***trimerization*** , or tetramerization domains failed to recapitulate
KRAB domain binding. Chimeric KAP-1-RBCC proteins containing either the
RING, RING-B box, or coiled-coil regions from MID1 also failed to bind the
KRAB domain. The KAP-1-RBCC mediates a highly specific, direct interaction
with the KRAB domain, and it appears to function as an integrated,
possibly cooperative structural unit wherein each sub-domain contributes
to oligomerization and/or ligand recognition. These observations provide
the first principles for RBCC domain-mediated protein-protein interaction
and have implications for identifying new ligands for RBCC domain
proteins. (C) 2000 Academic Press.

L6 ANSWER 10 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 7
ACCESSION NUMBER: 1999245702 EMBASE
TITLE: Disruption of coiled-coil domains in Fer protein-tyrosine
kinase abolishes trimerization but not kinase activation.
AUTHOR: Craig A.W.B.; Zirngibl R.; Greer P.
CORPORATE SOURCE: P. Greer, Cancer Research Labs, Botterell Hall, Queen's
University, Kingston, Ont. K7L 3N6, Canada.
greerp@post.queensu.ca
SOURCE: Journal of Biological Chemistry, (9 Jul 1999) 274/28
(19934-19942).
Refs: 53
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The protein-tyrosine kinase Fer and the highly homologous proto-
oncoprotein Fps/Fes are implicated in signaling from a variety of growth
factor and cytokine receptors. Here we examine the molecular basis of Fer
kinase activation with an emphasis on the role of oligomerization. We show
that Fer forms ***trimers*** in vivo and that disruption of either the
first or second coiled-coil domain abolishes oligomerization, suggesting a
cooperative interaction between these two domains. Although Fps/Fes also
forms homotypic oligomers, probably via homologous coiled-coil domains, no
heterotypic interactions were observed between Fer and Fps/Fes.
Incorporation of catalytically inactive Fer peptides into the oligomeric
complex caused only mild reduction of ***wild*** type Fer kinase
activity, suggesting that kinase- inactive Fer would not behave as a
potent ***dominant*** ***negative*** . Although oligomerization of
Fer can potentiate autophosphorylation in trans at three major
phosphorylation sites, these residues can likely also be phosphorylated in
cis. In contrast, the testis-specific FerT isomer does not oligomerize and
is able to autophosphorylate in cis at two of the same three residues
autophosphorylated in Fer. These results suggest that although
oligomerization potentiates autophosphorylation in trans, this is
apparently not necessary for Fer activation.

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on STN DUPLICATE 8
ACCESSION NUMBER: 1999111160 EMBASE
TITLE: Fas ligand-independent, FADD-mediated activation of the Fas
death pathway by anticancer drugs.
AUTHOR: Micheau O.; Solary E.; Hammann A.; Dimanche-Boitrel M.-T.
CORPORATE SOURCE: M.-T. Dimanche-Boitrel, INSERM U517, Pole Biol./Therapie
Cancers (JE 515), Faculty of Medicine and Pharmacy, 7
boulevard Jeanne d'Arc, 21033 Dijon Cedex, France.
mtboitre@u-bourgogne.fr
SOURCE: Journal of Biological Chemistry, (19 Mar 1999) 274/12
(7987-7992).
Refs: 31
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ***Trimerization*** of the Fas receptor (CD95, APO-1), a membrane
bound protein, triggers cell death by apoptosis. The main death pathway
activated by Fas receptor involves the adaptor protein FADD (for

Fas-associated death domain) that connects Fas receptor to the caspase cascade. Anticancer drugs have been shown to enhance both Fas receptor and Fas ligand expression on tumor cells. The contribution of Fas ligand-Fas receptor interactions to the cytotoxic activity of these drugs remains controversial. Here, we show that neither the antagonistic anti-Fas antibody ZB4 nor the Fas-IgG molecule inhibit drug-induced apoptosis in three different cell lines. The expression of Fas ligand on the plasma membrane, which is identified in untreated U937 human leukemic cells but remains undetectable in untreated HT29 and HCT116 human colon cancer cell lines, is not modified by exposure to various cytotoxic agents. These drugs induce the clustering of Fas receptor, as observed by confocal laser scanning microscopy, and its interaction with FADD, as demonstrated by co-immunoprecipitation. Overexpression of FADD by stable transfection sensitizes tumor cells to drug-induced cell death and cytotoxicity, whereas down-regulation of FADD by transient transfection of an antisense construct decreases tumor cell sensitivity to drug-induced apoptosis. These results were confirmed by transient transfection of constructs encoding either a FADD ***dominant*** ***negative*** ***mutant*** or MC159 or E8 viral proteins that inhibit the FADD/caspase-8 pathway. These results suggest that drug-induced cell death involves the Fas/FADD pathway in a Fas ligand-independent fashion.

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on STN
ACCESSION NUMBER: 1999189724 EMBASE
TITLE: Down-regulation of cyclin B1 gene transcription in terminally differentiated skeletal muscle cells is associated with loss of functional CCAAT-binding NF-Y complex.
AUTHOR: Farina A.; Manni I.; Fontemaggi G.; Tiainen M.; Cenciarelli C.; Bellorini M.; Mantovani R.; Sacchi A.; Piaggio G.
CORPORATE SOURCE: G. Piaggio, Laboratorio di Oncogenesi Molecolare, (CRS-IRE), Via delle Messi D'Oro 156, 00158 Roma, Italy
SOURCE: Oncogene, (6 May 1999) 18/18 (2818-2827).
Refs: 45
ISSN: 0950-9232 CODEN: ONCNES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The observation that cyclin B1 protein and mRNAs are down-regulated in terminally differentiated (TD) C2C12 cells, suggested us to investigate the transcriptional regulation of the cyclin B1 gene in these cells. Transfections of cyclin B1 promoter constructs indicate that two CCAAT boxes support cyclin B1 promoter activity in proliferating cells. EMSAs demonstrate that both CCAAT boxes are recognized by the ***trimeric*** NF-Y complex in proliferating but not in TD cells. Transfecting a ***dominant*** - ***negative*** ***mutant*** of NF-YA we provide evidence that NF-Y is required for maximal promoter activity. Addition of recombinant NF-YA to TD C2C12 nuclear extracts restores binding activity in vitro, thus indicating that the loss of NF-YA in TD cells is responsible for the lack of the NF-Y binding to the CCAAT boxes. Consistent with this, we found that the NF-YA protein is absent in TD C2C12 cells. In conclusion, our data demonstrate that NF-Y is required for cyclin B1 promoter activity. We also demonstrate that cyclin B1 expression is regulated at the transcriptional level in TD C2C12 cells and that the switch-off of cyclin B1 promoter activity in differentiated cells depends upon the loss of a functional NF-Y complex. In particular the loss of NF-YA protein is most likely responsible for its inactivation.

L6 ANSWER 13 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999256690 EMBASE
TITLE: Assembly of a novel cartilage matrix protein filamentous network: Molecular basis of differential requirement of von Willebrand factor A domains.
AUTHOR: Chen Q.; Zhang Y.; Johnson D.M.; Goetinck P.F.
CORPORATE SOURCE: Q. Chen, Musculoskeletal Research Laboratory, Dept. of Orthopaedics/Rehabilitation, Pennsylvania State University, Hershey, PA 17033, United States. qchen@ortho.hmc.psu.edu
SOURCE: Molecular Biology of the Cell, (1999) 10/7 (2149-2162).
Refs: 34
ISSN: 1059-1524 CODEN: MBCEEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cartilage matrix protein (CMP) is the prototype of the newly discovered matrilin family, all of which contain yon Willebrand factor A domains.

Although the function of matrilins remain unclear, we have shown that, in primary chondrocyte cultures, CMP (matrilin-1) forms a filamentous network, which is made up of two types of filaments, a collagen-dependent one and a collagen-independent one. In this study, we demonstrate that the collagen- independent CMP filaments are enriched in pericellular compartments, extending directly from chondrocyte membranes. Their morphology can be distinguished from that of collagen filaments by immunogold electron microscopy, and mimicked by that of self-assembled purified CMP. The assembly of CMP filaments can occur from transfection of a ***wild*** -type CMP transgene alone in skin fibroblasts, which do not produce endogenous CMP. Conversely, assembly of endogenous CMP filaments by chondrocytes can be inhibited specifically by ***dominant*** ***negative*** CMP transgenes. The two A domains within CMP serve essential but different functions during network formation. Deletion of the A2 domain converts the ***trimeric*** CMP into a mixture of monomers, dimers, and ***trimers*** , whereas deletion of the A1 domain does not affect the ***trimeric*** configuration. This suggests that the A2 domain modulates multimerization of CMP. Absence of either A domain from CMP abolishes its ability to form collagen-independent filaments. In particular, Asp22 in A1 and Asp255 in A2 are essential; double point mutation of these residues disrupts CMP network formation. These residues are part of the metal ion- dependent adhesion sites, thus a metal ion-dependent adhesion site-mediated adhesion mechanism may be applicable to matrilin assembly. Taken together, our data suggest that CMP is a bridging molecule that connects matrix components in cartilage to form an integrated matrix network.

L6 ANSWER 14 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999112263 EMBASE
TITLE: The cyclin B2 promoter depends on NF-Y, a trimer whose CCAAT-binding activity is cell-cycle regulated.
AUTHOR: Bolognese F.; Wasner M.; Lange-zu Dohna C.; Gurtner A.; Ronchi A.; Muller H.; Manni I.; Mossner J.; Piaggio G.; Mantovani R.; Engeland K.
CORPORATE SOURCE: R. Mantovani, Dipt. Gen. Biologia Microrganism, Univesita di Milano, Via Celoria 26, 20133 Milano, Italy
SOURCE: Oncogene, (11 Mar 1999) 18/10 (1845-1853).
Refs: 52
ISSN: 0950-9232 CODEN: ONCNES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cyclin B2 is a regulator of p34cdc2 kinase, involved in G2/M progression of the cell cycle, whose gene is strictly regulated at the transcriptional level in cycling cells. The mouse promoter was cloned and three conserved CCAAT boxes were found. In this study, we analysed the mechanisms leading to activation of the cyclin B2 CCAAT boxes: a combination of (i) genomic footprinting, (ii) transfections with single, double and triple ***mutants*** , (iii) EMSAs with nuclear extracts, antibodies and NF-Y recombinant proteins and (iv) transfections with an NF-YA ***dominant*** ***negative*** ***mutant*** established the positive role of the three CCAAT sequences and proved that NF-Y plays a crucial role in their activation. NF-Y, an ubiquitous ***trimer*** containing histone fold subunits, activates several other promoters regulated during the cell cycle. To analyse the levels of NF-Y subunits in the different phases of the cycle we separated MEL cells by elutriation, obtaining fractions > 80% pure. The mRNA and protein levels of the histone-fold containing NF-YB and NF-YC were invariant, whereas the NF-YA protein, but not its mRNA, was maximal in mid-S and decreased in G2/M. EMSA confirmed that the CCAAT-binding activity followed the amount of NF-YA, indicating that this subunit is limiting within the NF-Y complex, and suggesting that post-transcriptional mechanisms regulate NF-YA levels. Our results support a model whereby fine tuning of this activator is important for phase-specific transcription of CCAAT-containing promoters.

L6 ANSWER 15 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999295218 EMBASE
TITLE: Dominant negative mutations in the .alpha.-factor receptor, a G protein-coupled receptor encoded by the STE2 gene of the yeast Saccharomyces cerevisiae.
AUTHOR: Leavitt L.M.; Macaluso C.R.; Kim K.S.; Martin N.P.; Dumont M.E.
CORPORATE SOURCE: M.E. Dumont, Department Biochemistry Biophysics, University Rochester Medical Center, 575 Elmwood Avenue, Rochester, NY

14642, United States
SOURCE: Molecular and General Genetics, (1999) 261/6 (917-932).
Refs: 65
ISSN: 0026-8925 CODEN: MGGEAE
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The .alpha.-mating pheromone receptor encoded by the STE2 gene of the yeast Saccharomyces cerevisiae is a G protein-coupled receptor (GPCR) that is homologous to the large family of GPCRs that mediate multiple types of signal transduction in mammals. We have screened libraries of ***mutant*** receptors to identify ***dominant*** ***negative*** alleles that are capable of interfering with the function of a co-expressed normal receptor. Two ***dominant*** ***negative*** alleles have been recovered in this manner. In addition, we find that previously isolated loss-of-function mutations in the .alpha.-factor receptor exhibit ***dominant*** ***negative*** effects. Detection of the dominant effects requires high-level expression of the ***mutant*** receptors but does not require a high ratio of ***mutant*** to normal receptors. Cellular levels of the normal receptors are not affected by co-expression of the ***dominant*** ***negative*** alleles. Expression of the ***mutant*** receptors does not interfere with constitutive signaling in a strain that lacks the G protein .alpha. subunit encoded by GPA1, indicating that interference with signaling occurs at the level of the receptor or the interacting G protein. Expression of increased levels of G protein subunits partially reverses the ***dominant*** ***negative*** effects. The ***dominant*** ***negative*** behavior of the ***mutant*** receptors is diminished by deletion of the SST2 gene, which encodes an RGS (Regulator of G protein Signaling) protein involved in desensitization of pheromone signaling. The most likely explanation for the ***dominant*** ***negative*** effects of the mutations appears to be the existence of an interaction between unactivated receptors and the ***trimeric*** G protein that titrates the G protein away from the normal receptors or renders the G protein insensitive to receptor activation. This interaction appears to be mediated by the SST2 gene product.

L6 ANSWER 16 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999046957 EMBASE
TITLE: A G(s.alpha.) mutant designed to inhibit receptor signaling through G(s).
AUTHOR: Iiri T.; Bell S.M.; Baranski T.J.; Fujita T.; Bourne H.R.
CORPORATE SOURCE: H.R. Bourne, Box 0450, Univ. of California Medical Center, San Francisco, CA 94143, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (19 Jan 1999) 96/2 (499-504).
Refs: 42
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hormonal signals activate ***trimeric*** G proteins by substituting GTP for GDP bound to the G protein .alpha. subunit (G.alpha.), thereby generating two potential signaling molecules, G.alpha.-GTP and free G.beta..gamma.. The usefulness of ***dominant*** ***negative*** mutations for investigating Ras and other monomeric G proteins inspired us to create a functionally analogous ***dominant*** ***negative*** G.alpha. mutation. Here we describe a ***mutant*** .alpha. subunit designed to inhibit receptor- mediated hormonal activation of G(s), the stimulatory regulator of adenylyl cyclase. To construct this ***mutant*** , we introduced into the .alpha. subunit ({s) of G(s) three separate mutations chosen because they impair as function in complementary ways: the A366S ***mutant*** reduces affinity of as for binding GDP, whereas the G226A and E268A mutations impair the protein's ability to bind GTP and to assume an active conformation. The triple ***mutant*** robustly inhibits (by up to 80%) G(s)-dependent hormonal stimulation of adenylyl cyclase in cultured cells. Inhibition is selective in that it does not affect cellular responses to expression of a constitutively active {s) ***mutant*** (.alpha.(s)-R201C) or to agonists for receptors that activate G(q) or Gi. This .alpha.(s) triple ***mutant*** and cognate G.alpha. ***mutants*** should provide specific tools for dissection of G protein-mediated signals in cultured cells and transgenic animals.

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on STN
ACCESSION NUMBER: 1998137970 EMBASE
TITLE: Effect of cleavage mutants on syncytium formation directed
by the wild- type fusion protein of newcastle disease
virus.
AUTHOR: Li Z.; Sergel T.; Razvi E.; Morrison T.
CORPORATE SOURCE: T. Morrison, Dept. of Molec. Genetics/Microbiol., Univ. of
Massachusetts Med. School, 55 Lake Ave. North, Worcester,
MA 01655, United States.
trudy.morrison@banyan.ummed.edu
SOURCE: Journal of Virology, (1998) 72/5 (3789-3795).
Refs: 29
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The effects of Newcastle disease virus (NDV) fusion (F) glycoprotein
cleavage ***mutants*** on the cleavage and syncytium-forming activity
of the ***wild*** - type F protein were examined. F protein cleavage
mutants were made by altering amino acids in the furin recognition
region (amino acids 112 to 116) in the F protein of a virulent strain of
NDV. Four ***mutants*** were made: Q114P replaced the glutamine
residue with proline; K115G replaced lysine with glycine; double
mutant K115G, R113G replaced both a lysine and an arginine with
glycine residues; and a triple ***mutant*** , R112G, K115G, F117L,
replaced three amino acids to mimic the sequence found in avirulent
strains of NDV. All ***mutants*** except Q114P were cleavage negative
and fusion negative. However, addition of exogenous trypsin cleaved all
mutant F proteins and activated fusion. As expected for an
oligomeric protein, the fusion-negative ***mutants*** had a
dominant ***negative*** phenotype: cotransfection of
wild -type and ***mutant*** F protein cDNAs resulted in an
inhibition of syncytium formation. The presence of the ***mutant*** F
protein did not inhibit cleavage of the ***wild*** -type protein.
Furthermore, evidence is presented that suggests that the ***mutant***
protein and the ***wild*** -type protein formed heterooligomers. By
measuring the syncytium-forming activity of the ***wild*** -type
protein at various ratios of expression of ***mutant*** and
wild -type protein, results were obtained that are most consistent
with the notion that the size of the functionally active NDV F protein in
these assays is a single oligomer, likely a ***trimer*** . That a
larger oligomer, containing a mix of both ***wild*** -type and
mutant F proteins, has partial activity cannot, however, be ruled
out.

L6 ANSWER 18 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 9
ACCESSION NUMBER: 1998114791 EMBASE
TITLE: A naturally occurring isoform of the human macrophage
scavenger receptor (SR-A) gene generated by alternative
splicing blocks modified LDL uptake.
AUTHOR: Gough P.J.; Greaves D.R.; Gordon S.
CORPORATE SOURCE: P.J. Gough, Sir William Dunn School of Pathology,
University of Oxford, South Parks Road, Oxford OX1 3RE,
United Kingdom
SOURCE: Journal of Lipid Research, (1998) 39/3 (531-543).
Refs: 36
ISSN: 0022-2275 CODEN: JLPRAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The class A macrophage scavenger receptors (SPA) are macrophage-specific
trimeric integral membrane glycoproteins that have been implicated
in many macrophageassociated physiological and pathological processes
including atherosclerosis, Alzheimer's disease, and host defense. There
are two forms of the receptor that have been previously cloned, and both
are generated by alternative splicing of a single gene. Here we report the
cloning of a third, alternatively spliced isoform of the human SR-A gene
(type III hSRA). The novel isoform is expressed in the human monocytic
leukemia cell line THP-1 and also in primary human monocyte derived
macrophages. When expressed in CHO-K1 cells, type III hSR-A does not
internalize AcLDL despite having the domain shown to mediate this function
in type I and II hSR-A. We show that type III protein has altered
intracellular processing and is trapped within the endoplasmic reticulum,
making it unable to perform endocytosis. Type III protein acts as a
dominant ***negative*** isoform by reducing modified LDL
uptake in CHO cells stably expressing either type I or type II SR-A. The

demonstration that a naturally occurring splice ***variant*** of SR-A
mRNA can act as a ***dominant*** ***negative*** isoform suggests a
novel mechanism for regulation of scavenger receptor activity in
macrophages.

L6 ANSWER 19 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1998316914 EMBASE
TITLE: Possible existence of quaternary structure in the
high-affinity serotonin transport complex.
AUTHOR: Chang A.S.; Starnes D.M.; Chang S.M.
CORPORATE SOURCE: Dr. A.S. Chang, CWRU School of Medicine, 17815 Lakewood
Heights Boulevard, Lakewood, OH 44107, United States.
asc6@po.cwru.edu
SOURCE: Biochemical and Biophysical Research Communications, (19
Aug 1998) 249/2 (416-421).
Refs: 32
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Deletion- ***mutants*** of the cloned mouse serotonin transporter
(SERT) rendered ***dominant*** ***negative*** -***mutant***
effects upon ***wild*** -type transporter activities in heterologous
expression studies; such effects were transporter-selective and did not
influence the activities of co-expressed neuronal GABA transporter.
Heterologous expression of linear concatenates (up to four copies) of SERT
further revealed discernable uptake activities for both transporter-dimer
and -tetramer, but not for the ***trimer*** . Kinetic and
pharmacological analyses revealed that the monomer, dimer, and tetramer
manifested comparable transport K(m) and potencies for known serotonin
uptake inhibitors; the tetramer was distinct from the others only in
manifesting notably reduced transport V(max). Surprisingly, equivalent
cocaine congener-binding activities were observed for all concatenates,
including the functionally inactive ***trimer*** . These findings
collectively support the existence of quaternary structure in the active
5-HT transport complex; such structure is likely to be a critical
determinant of ligand transport activities, but apparently not of
transporter-inhibitor interactions.

L6 ANSWER 20 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 97192665 EMBASE
DOCUMENT NUMBER: 1997192665
TITLE: An evaluation of strategies available for the
identification of GTP-binding proteins required in
intracellular signalling pathways.
AUTHOR: Barritt G.J.; Gregory R.B.
CORPORATE SOURCE: G.J. Barritt, Department of Medical Biochemistry, School of
Medicine, Flinders University, GPO Box 2100, Adelaide, SA
5001, Australia
SOURCE: Cellular Signalling, (1997) 9/3-4 (207-218).
Refs: 115
ISSN: 0898-6568 CODEN: CESIEY
PUBLISHER IDENT.: S 0898-6568(96)00131-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Strategies which can be used to elucidate the nature of a GTP-binding
regulatory protein (G-protein) involved in an intracellular pathway of
interest in the complex environment of the cell are described and
evaluated. A desirable strategy is considered to be one in which the first
stage indicates a requirement for one or more G-proteins, provides
information on whether a monomeric, ***trimeric*** or other type of
G-protein is involved, and gives some idea of the G protein sub-class. In
the second stage the specific G-protein involved is identified. Approaches
available for investigations in the first stage include the use of
analogues of GTP and GDP, AlF4-, inhibitors of G-protein isoprenylation,
bacterial toxins which covalently modify G-proteins, and the introduction
of a purified GDP dissociation inhibitor, GDP exchange and/or GTP-ase
activating protein. Identification of the specific G-protein in the second
stage can be achieved using anti G-protein antibodies, G-protein- or
receptor-derived peptides, antisense G protein RNA and over-expressed,
constitutively-active or ***dominant*** -***negative*** G-protein
mutants . The correct interpretation of results obtained with GTP
and GDP analogues and AlF4- in the first stage is complex and often
difficult, and requires a thorough understanding of the functions and
mechanisms of activation of G-proteins. Nevertheless, it is important to
reach the correct conclusion at this stage since considerable time and
expense are usually required for investigations in the second stage.

L6 ANSWER 21 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 97334294 EMBASE
DOCUMENT NUMBER: 1997334294
TITLE: Deletion mutants of the herpes simplex virus type 1 UL8
protein: Effect on DNA synthesis and ability to interact
with an influence the intracellular localization of the UL5
and UL52 proteins.
AUTHOR: Barnard E.C.; Brown G.; Stow N.D.
CORPORATE SOURCE: N.D. Stow, MRC Virology Unit, Institute of Virology, Church
Street, Glasgow G11 5JR, United Kingdom.
n.stow@vir.gla.ac.uk
SOURCE: Virology, (1997) 237/1 (97-106).
Refs: 42
ISSN: 0042-6822 CODEN: VIRLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The herpes simplex virus type 1 (HSV-1) helicase-primase, an essential
component of the viral DNA replication machinery, is a ***trimeric***
complex of the virus-coded UL5, UL8, and UL52 proteins. An assembly of the
UL5 and UL52 subunits retains both enzymic activities, and the UL3 protein
has been implicated in modulating these functions, facilitating efficient
nuclear uptake of the complex and interacting with other viral DNA
replication proteins. To further our understanding of UL8, we have
constructed plasmids expressing ***mutant*** proteins, truncated at
their N- or C-termini or lacking amino acids internally, under the control
of the human cytomegalovirus major immediate-early promoter. Deletion of
23 amino acids from the N-terminus or 33 from the C-terminus abolished the
ability of UL8 to support DNA replication in transient transfection
assays. None of the UL8 ***mutants*** tested exhibited a strong
dominant ***negative*** phenotype in the presence of the
wild -type product, although some inhibition of replication was
observed with ***mutants*** lacking 165 N-terminal or 497 C-terminal
amino acids. The ability of the UL8 ***mutants*** to facilitate
efficient nuclear localization of UL52 in the presence of coexpressed UL5
was examined by immunofluorescence. Selected ***mutants*** were also
expressed by recombinant baculoviruses and tested for Interaction with UL5
and UL52 in immunoprecipitation assays. The replicative ability of the
mutants was found to correlate with their ability to localize UL52
to the nucleus, but not their interaction with UL5 and UL52. This property
precluded the identification of any region of UL8 important for its
presumed nuclear functions.

L6 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:301161 CAPLUS
DOCUMENT NUMBER: 126:342347
TITLE: Functional and mutational analysis of Fas receptor
(CD95) in three patients with autoimmune
lymphoproliferative syndrome
AUTHOR(S): Wada, Taizo
CORPORATE SOURCE: Department Pediatrics, School Medicine, Faculty
Medicine, Kanazawa University, Kanazawa, 920, Japan
SOURCE: Kanazawa Daigaku Juzen Igakkai Zasshi (1996), 105(6),
776-787
CODEN: JUZIAG; ISSN: 0022-7226
PUBLISHER: Juzen Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The Fas receptor/Fas ligand system induces apoptosis of Fas-bearing cells
and plays an important role in the immune regulations, esp. in the
deletion of self-reactive clones. It is known that lpr mice caused by the
Fas deficiency exhibit autoimmunity with abnormal proliferation of
CD4-CD8- (double-neg.) T cells. Autoimmune lymphoproliferative syndrome
(ALPS) was recently identified as a human counterpart of the lpr mouse.
In this study, 3 cases of ALPS from two independent families were
evaluated for immunol. and genetic abnormalities of the Fas receptor.
They all exhibited lymphoadenopathy, hepatosplenomegaly, thrombocytopenia,
hypergammaglobulinemia and the increased no. of double-neg. T cells from
early childhood. In patients 1 and 2 (family 1) who were heterozygous in
the Fas receptor gene, the genomic sequence of the mutant allele inherited
from their mother showed a T to C point mutation in the 5' splice site of
intron 7, resulting in aberrant splicing. In the mutant mRNA, 4 bases
insertion (GCAG) between exon 7 and 8 was predicted to cause a frameshift
and premature termination after 9 missense codons. The surface Fas
expression on activated T cells from these patients was comparable to that
on normal T cells, but the truncated ***mutant*** proteins lacking the
death domain probably induced a ***dominant*** ***neg*** . effect,
leading to the formation fo abnormal ***trimers*** unable to transduce

the intracytoplasmic death signal. Although their mother had an identical
mutation of the Fas receptor and exhibited a similar resistance to
Fas-mediated apoptosis at the cellular level, she remained asymptomatic.
These facts suggested that there exists an addnl. factor responsible for
the manifestation of typical ALPS. Patient 3 (family 2) was born to
parents who were cousins, and the genomic sequence of the homozygous
mutant alleles showed an A to G point mutation in the 3' splice site of
the intron 3. The mRNA lacking exon 4 was predicted to have a frameshift
and premature termination after 38 missense codons. Absence of the Fas
expression may preclude any Fas-mediated signals and result in much
severer clin. features in this case. In all cases, activation-induced
cell death of T cells was markedly diminished and Fas-induced apoptosis
was defective. It was strongly suggested that these abnormalities of the
T cell function led to the failure in the exclusion of self-reactive T
cell clones, resulting in the development of various autoimmune disorders.
Moreover, decreased Fas-mediated apoptosis of cultured B cells from these
patients suggested that defective killing of the self-reactive B cells was
directly related to the hypergammaglobulinemia and the autoantibody prodn.

L6 ANSWER 23 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 96025328 EMBASE
DOCUMENT NUMBER: 1996025328
TITLE: PTP1D is a positive regulator of the prolactin signal
leading to .beta.-casein promoter activation.
AUTHOR: Ali S.; Chen Z.; Lebrun J.-J.; Vogel W.; Kharitonenkov A.;
Kelly P.A.; Ullrich A.
CORPORATE SOURCE: Department of Molecular Biology, Max-Planck-Institut fur
Biochemie, Am Klopferspitz 18A,82152 Martinsried, Germany
SOURCE: EMBO Journal, (1996) 15/1 (135-142).
ISSN: 0261-4189 CODEN: EMJODG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Stimulation of the prolactin receptor (PRLR), a member of.the
cytokine/growth hormone receptor family, results in activation of the
associated Jak2 tyrosine kinase and downstream signaling pathways. We
report that PTP1D, a cytoplasmic protein tyrosine phosphatase containing
two Src homology 2 (SH2) domains, physically associates with the PRLR-Jak2
complex and is tyrosine-phosphorylated upon stimulation with prolactin.
The formation of the ***trimeric*** PRLR-Jak2-PTP1D complex is
critical for transmission of a lactogenic signal, while PTP1D
phosphorylation is necessary, but not sufficient. The ***dominant***
negative inhibitory effect of a phosphatase-deficient
mutant on expression of a .beta.-casein promoter-controlled
reporter gene is evidence for an essential role of fully functional PTP1D
in the regulation of milk protein gene transcription.

L6 ANSWER 24 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 10
ACCESSION NUMBER: 96001797 EMBASE
DOCUMENT NUMBER: 1996001797
TITLE: Dominant-negative mutants of Grb2 induced reversal of the
transformed phenotypes caused by the point
mutation-activated rat HER-2/neu.
AUTHOR: Xie Y.; Pendergast A.M.; Hung M.-C.
CORPORATE SOURCE: Department of Tumor Biology, Texas Univ. M. D. Anderson
Can. Ctr.,Houston, TX 77030, United States
SOURCE: Journal of Biological Chemistry, (1995) 270/51
(30717-30724).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To clarify the role of the Shc-Grb2-Sos ***trimer*** in the oncogenic
signaling of the point mutation-activated HER-2/neu receptor tyrosine
kinase (named p185), we interfered with the protein-protein interactions
in the Shc-Grb2- Sos complex by introducing Grb2 ***mutants*** with
deletions in either amino- (.DELTA.N- Grb2) or carboxyl(.delta.C-Grb2)
terminal SH3 domains into B104-1-1 cells derived from NIH3T3 cells
expressing the point mutation-activated HER-2/neu. We found that the
transformed phenotypes of the B104-1-1 cells were largely reversed by the
.DELTA.N-Grb2. The effect of the .DELTA.C-Grb2 was much weaker.
Biochemical analysis showed that the AN-Grb2 was able to associate Shc but
not p185 or Sos, while the .DELTA.C-Grb2 bound to Shc, p185, and Sos. The
p185-mediated Ras activation was severely inhibited by the .DELTA.N-Grb2
but not the .DELTA.C-Grb2. Taken together, these data demonstrate that

interruption of the interaction between Shc and the endogenous Grb2 by the
.DELTA.N-Grb2 impairs the oncogenic signaling of the activated p185,
indicating that (i) the .DELTA.N-Grb2 functions as a strong
dominant - ***negative*** ***mutant*** , and (ii)
Shc/Grb2/Sos pathway plays a major role in mediating the oncogenic signal
of the activated p185. Unlike the AN-Grb2, .DELTA.C-Grb2 appears to be a
relatively weak ***dominant*** - ***negative*** ***mutant*** ,
probably due to its ability to largely fulfill the biological functions of
the ***wild*** - type Grb2.

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on STN
ACCESSION NUMBER: 95290825 EMBASE
DOCUMENT NUMBER: 1995290825
TITLE: Purification and characterization of the G203T mutant
. .alpha.(i-2) subunit of GTP-binding protein expressed in
baculovirus-infected sf9 cells.
AUTHOR: Inoue S.-I.; Hoshino S.-I.; Kukimoto I.; Ui M.; Katada T.
CORPORATE SOURCE: Dept. Physiological Chemistry, Faculty of Pharmaceutical
Sciences, The University of Tokyo,Hongo, Bunkyo-ku, Tokyo
113, Japan
SOURCE: Journal of Biochemistry, (1995) 118/3 (650-657).
ISSN: 0021-924X CODEN: JOBIAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry .
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We expressed the Gly203.fwdarw.Thr (G203T) ***mutant*** of
G(i2).alpha., which was expected to show a ***dominant*** -
negative phenotype in G(i2)-mediated signal transduction, in
baculovirus-infected Sf9 cells and purified the ***mutant*** at
subunit for its characterization. The rate of dissociation of GDP from
G203T G(i2).alpha. was 3- to 4-fold faster than that from ***wild***
-type G(i2).alpha. but their k(cat) values for GTP hydrolysis were almost
the same. The affinities of the two G(i2).alpha. proteins for the
.beta..gamma. subunits of G proteins to form .alpha..beta..gamma.
trimers , which served as substrates for pertussis toxin-catalyzed
ADP-ribosylation, were the same. In marked contrast, G203T G(i2).alpha.
was unable to form a tight complex with a non-hydrolyzable analog
(GTP[.gamma.S]) of GTP; bound GTP[.gamma.S] was readily released from the
mutant G(i2).alpha. even in the presence of a high concentration
of Mg2+. Its susceptibility to tryptic digestion also revealed that
GTP[.gamma.S]-bound G203T G(i2).alpha. formed a conformation apparently
different from that of the GTP[.gamma.S]-bound form of ***wild*** -type
G(i2).alpha.. Both the G203T and ***wild*** -type G(i2).alpha. proteins
were capable of coupling with membrane-bound .alpha.-adrenergic receptors,
resulting in the formation of receptor-.alpha. protein complexes with high
affinity for agonists. However, GTP[.gamma.S]-dependent uncoupling from
the high-affinity receptors was markedly attenuated in the case of G203T
G(i2).alpha.. Thus, G203T-mutated G(i2).alpha. had a unique property in
terms of coupling to membrane receptors, in addition to the previously
expected defect in the active conformation of the GTP-bound form of
G(i2).alpha..

L6 ANSWER 26 OF 31 MEDLINE on STN
DUPLICATE 11
ACCESSION NUMBER: 95268420 MEDLINE
DOCUMENT NUMBER: 95268420 PubMed ID: 7749409
TITLE: Concentration of mutations causing Schmid metaphyseal
chondrodysplasia in the C-terminal noncollagenous domain of
type X collagen.
AUTHOR: McIntosh I; Abbott M H; Francomano C A
CORPORATE SOURCE: Department of Medicine, Johns Hopkins University School of
Medicine, Baltimore, Maryland 21287, USA.
SOURCE: HUMAN MUTATION, (1995) 5 (2) 121-5.
Journal code: 9215429. ISSN: 1059-7794.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19950629
Entered Medline: 19950621
AB Schmid metaphyseal chondrodysplasia (SMCD) has previously been shown to be
the result of mutations in the type X collagen gene, COL10A1. A further
three mutations have been identified, including two nonsense mutations
(Y268X, W651X) and a frameshift mutation (1856delCC). Each of the 10 SMCD
mutations identified to date is within the C-terminal noncollagenous
domain of type X collagen and three of five deletions initiated around the
same nucleotide. This domain is believed to be involved in the initiation
of collagen trimerization. The concentration of mutations within this

domain is consistent with the hypothesis that the phenotype is the result
of a reduction in the level of mature type X collagen due to the
mutant polypeptide's inability to participate in ***trimer***
formation, although a ***dominant*** - ***negative*** mechanism
cannot be discounted, on the basis of current evidence.

L6 ANSWER 27 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 12
ACCESSION NUMBER: 93206694 EMBASE
DOCUMENT NUMBER: 1993206694
TITLE: Characterization of an arginine 789 to cysteine
substitution in .alpha.1 (II) collagen chains of a patient
with spondyloepiphyseal dysplasia.
AUTHOR: Chan D.; Taylor T.K.F.; Cole W.G.
CORPORATE SOURCE: Division of Orthopaedics, Hospital for Sick Children, 555
University Ave.,Toronto, Ont. M5G 1X8, Canada
SOURCE: Journal of Biological Chemistry, (1993) 268/20
(15238-15245).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A child with spondyloepiphyseal dysplasia congenita was shown to be
heterozygous for a mutation of the COL2A1 gene that encodes the
.alpha.1(II) chain of type II collagen. The .alpha.1(II) chains extracted
from cartilage contained disulfide-bonded dimeric and ***trimeric***
.alpha.1(II) chains. Carboxymethylation confirmed that some of the type II
collagen chains contained cysteine residues that are not normally present
in .alpha.1(II) chains. Cyanogen bromide peptide mapping showed that the
abnormal cysteine residue was located in the .alpha.1(II) CB10.5 peptide.
Amplification products of the corresponding region of .alpha.1(II) cDNA
prepared from cultured dermal fibroblasts were shown by chemical cleavage
and single strand conformation polymorphism analyses to contain a sequence
anomaly. DNA sequencing showed a transition of C2913T in exon 41 of one
allele of the COL2A1 gene resulting in the substitution of arginine 789 by
cysteine in the .alpha.1(II) chain. The mutation resulted in the loss of a
MaeII cleavage site that was used to confirm that the proband was
heterozygous for the mutation and that neither parent showed evidence of
the mutation. The type II collagen extracted from cartilage and from
chondrocytes cultured in alginate beads showed similar characteristics.
Approximately a third of the type II collagen chains were ***mutant***
, and the secretion of molecules containing ***mutant*** chains was
impaired. The thermal stability of the collagen extracted from cartilage
was normal. This study confirmed the importance of ***dominant***
negative mutations of the COL2A1 gene in producing the
spondyloepiphyseal dysplasia congenita phenotype.

L6 ANSWER 28 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 93070994 EMBASE
DOCUMENT NUMBER: 1993070994
TITLE: The collagenous domains of macrophage scavenger receptors
and complement component C1q mediate their similar, but not
identical, binding specificities for polyanionic ligands.
AUTHOR: Acton S.; Resnick D.; Freeman M.; Ekkel Y.; Ashkenas J.;
Krieger M.
CORPORATE SOURCE: Biology Department, Massachusetts Technology
Institute,Cambridge, MA 02139, United States
SOURCE: Journal of Biological Chemistry, (1993) 268/5 (3530-3537).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Macrophage scavenger receptors have been implicated in the development of
atherosclerosis and other macrophage-associated functions, including host
defense. The mechanism by which these receptors bind a wide array of
polyanions, such as acetylated low density lipoprotein (Ac-LDL), with high
affinity has not yet been elucidated; however, it has been proposed that
the positively charged extracellular collagenous domain of scavenger
receptors plays a key role in ligand binding. To test this proposal, we
generated truncation ***mutants*** of the bovine and murine scavenger
receptors and studied their expression in transiently transfected COS
cells. These ***mutants*** contain only 8 (bovine) or 5 (murine) of
the 24 Gly-X-Y tripeptide repeats found in the collagenous domains of the
full-length receptors. Immunochemical analyses established that the
truncation of the bovine scavenger receptor did not interfere
significantly with its synthesis, ***trimerization*** ,

post-translational processing, intracellular transport, surface
expression, or stability. However, unlike their full-length counterparts,
the truncated bovine and murine receptors were unable to bind Ac-LDL.
Thus, the collagenous domain was necessary for normal ligand binding. In
addition, cotransfection of the expression vector for the truncated bovine
scavenger receptor with that for the full-length receptor resulted in
dramatically reduced activity of the full-length construct (
dominant ***negative*** effect). A ligand bead-binding assay
was used to show that the isolated collagenous domain from a different
protein, complement component C1q, could bind a wide variety of polyanions
with a specificity which was similar, but not identical, to that of
scavenger receptors. These results suggest that the collagenous domain of
the scavenger receptor is both necessary and sufficient to determine the
broad binding specificity that characterizes this unusual receptor.
Scavenger receptors and C1q, along with the mannose-binding protein,
conglutinin, and lung surfactant apoprotein A, help define a set of
proteins which all contain short collagenous domains and which all appear
to participate in host defense. Their short collagenous domains may
contribute significantly to their host- defense functions.

L6 ANSWER 29 OF 31 MEDLINE on STN
DUPLICATE 13
ACCESSION NUMBER: 93054492 MEDLINE
DOCUMENT NUMBER: 93054492 PubMed ID: 1429567
TITLE: Negative complementation in aspartate transcarbamylase.
Analysis of hybrid enzyme molecules containing different
arrangements of polypeptide chains from wild-type and
inactive mutant catalytic subunits.
AUTHOR: Eisenstein E; Han M S; Woo T S; Ritchey J M; Gibbons I;
Yang Y R; Schachman H K
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of
California, Berkeley 94720.
CONTRACT NUMBER: GM 11067 (NIGMS)
GM 12159 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31)
22148-55.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921201
AB A comprehensive set of hybrid molecules of aspartate transcarbamylase
(ATCase) from Escherichia coli has been constructed of wild-type and
mutationally altered catalytic chains. The mutant enzymes that were
virtually devoid of activity contained a replacement of Gly-128 in the
catalytic polypeptide chains by either Asp or Arg. The kinetic properties
of these hybrid enzyme-like molecules were analyzed to evaluate the basis
for the unusual quaternary constraint demonstrated by an intersubunit
hybrid containing one wild-type catalytic subunit, one inactive mutant
subunit (containing the Gly to Asp replacement), and three wild-type
regulatory subunits. A similar intersubunit hybrid was constructed from
the wild-type catalytic subunit and the mutant in which Gly-128 was
replaced by Arg, and it too demonstrated a pronounced decrease in activity
relative to that expected for a hybrid containing three active sites.
Moreover, neither of these hybrid holoenzymes exhibited the cooperativity
with respect to aspartate that is characteristic of wild-type ATCase. In
contrast, hybrid holoenzymes containing at least one wild-type chain in
each catalytic subunit showed cooperativity. Also, hybrid enzymes
containing different arrangements of five, four, three, or two wild-type
catalytic chains with an appropriate complement of mutant chains had
specific activities proportional to the number of wild-type chains in the
holoenzymes. Exceptions were observed only in hybrids in which one of the
two subunits in the holoenzyme was composed completely of mutant catalytic
chains. For these hybrids the negative complementation was manifested as
a much lower enzyme activity than expected from the number of wild-type
chains in the enzyme and the loss of cooperativity. Thus, the activity
and allosteric properties of these hybrids is dependent on the arrangement
of catalytic chains in the holoenzyme, in contrast to results obtained for
hybrids containing native and chemically modified catalytic chains.
Intrasubunit hybrid catalytic ***trimers*** containing one or two
wild -type chains exhibited one-third and two-thirds the activity
of the intact ***wild*** -type catalytic subunit, respectively,
indicating the ***dominant*** ***negative*** effect that was seen
in intersubunit hybrid holoenzymes is absent within ***trimers*** :

L6 ANSWER 30 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 92354097 EMBASE
DOCUMENT NUMBER: 1992354097
TITLE: Human natriuretic peptide receptor-A guanylyl cyclase is
self-associated prior to hormone binding.
AUTHOR: Lowe D.G.
CORPORATE SOURCE: Department of Molecular Biology, Genentech, Inc., 460 Point
San Bruno Boulevard,South San Francisco, CA 94080, United
States
SOURCE: Biochemistry, (1992) 31/43 (10421-10425).
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The human natriuretic peptide receptor-A (NPR-A) guanylyl cyclase is
specifically activated to synthesize cGMP by binding of atrial natriuretic
peptide (ANP) to the receptor's extracellular domain. In this report,
NPR-A monoclonal and polyclonal antibodies were used to assess the
aggregation status of ***wild*** -type NPR-A and a truncation
mutant lacking most of the NPR-A cytoplasmic domain. On intact
human embryonic kidney 293 cells, in the absence of ANP, recombinant human
NPR-A is self-aggregated through disulfide bonds in an M(r) > 500 000,
possibly tetrameric, complex. Under nonreducing conditions, truncated
NPR-A was a monomer, indicating that the cytoplasmic domain is necessary
for NPR-A self-association. In the presence of the homobifunctional
cross-linker dithiobis(succinimidyl propionate), or disuccimidyl suberate,
truncated NPR-A could be cross-linked as a dimer and ***trimer*** only
in the presence of ANP. ***Wild*** -type NPR-A was cross-linked with
disuccinimidyl suberate to an M(r) > 500 000 species in the absence of
ANP, and with ANP, a smaller, M(r) .simeq.400 000 receptor ***trimer***
cross-linking product was observed, together with the larger, possibly
tetrameric complex. When whole cell stimulation of cGMP production by ANP
was tested on the low level of endogenous 293 cell NPR-A, maximal
stimulation was observed regardless of truncated NPR-A overexpression. The
absence of a ***dominant*** ***negative*** effect by the truncated
NPR-A, together with the cross-linking data, demonstrates that
preassociated NPR-A is the functionally relevant form of this receptor.

L6 ANSWER,31 OF 31 MEDLINE on STN
DUPLICATE 14
ACCESSION NUMBER: 93046647 MEDLINE
DOCUMENT NUMBER: 93046647 PubMed ID: 1423608
TITLE: The reovirus cell attachment protein possesses two
independently active trimerization domains: basis of
dominant negative effects.
AUTHOR: Leone G; Maybaum L; Lee P W
CORPORATE SOURCE: Department of Microbiology and Infectious Diseases,
University of Calgary Health Sciences Center, Alberta,
Canada.
SOURCE: CELL, (1992 Oct 30) 71 (3) 479-88.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 20021019
Entered Medline: 19921208
AB The reovirus cell attachment protein, sigma 1, is a homotrimer with an
N-terminal fibrous tail and a C-terminal globular head. By cotranslating
full-length and various truncated sigma 1 proteins in vitro, we show that
the N- and C-terminal halves of sigma 1 possess independent trimerization
and folding domains. Trimerization of sigma 1 is initiated at the
N-terminus by the formation of a "loose," protease-sensitive,
three-stranded, alpha-helical coiled coil. This serves to bring the three
unfolded C-termini into close proximity to one another, facilitating their
subsequent trimerization and cooperative folding. Concomitant with, but
independent of, this latter process, the N-terminal fiber further matures
into a more stable and protease-resistant structure. The coordinated
folding of sigma 1 ***trimers*** exemplifies the ***dominant***
negative effects of ***mutant*** subunits in oligomeric
complexes.

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S2037		USPT	variant$ or mutant$ or mutein$ or wild	☐
S2036		USPT	trimer$	☐
S2035		USPT	tnf or (tumor adj necrosis adj factor)	☐
S2034		USPT	tnf or (tumor adj necrosis adj factor)	☐
S2033		USPT	(mix? or combin$ or recombin$) and (mutant$ or mutein$ or variant$ or wild$) and (trimer$) and (dominant-negative or dominant adj negative)	☐
S2032		USPT	((mix? or combin$ or recombin$)same (mutant$ or mutein$ or variant$ or wild$	☐

			)) same (trimer$)	
S2031		USPT.	(mix? or combin$ or recombin$) same (mutant$ or mutein$ or variant$ or wild$)	☐
S2030		USPT	mix? or combin$ or recombin$	☐
S2029		USPT	((mutant$ or mutein$ or variant$ or wild$)and (trimer$)) and (dominant-negative or dominant adj negative)	☐
S2028		USPT	((mutant$ or mutein$ or variant$ or wild$)and (trimer$)) and (trimer$)	☐
S2027		USPT	(mutant$ or mutein$ or variant$ or wild$) and (trimer$)	☐
S2026		USPT	(dominant-negative or dominant adj negative) same ((mutant$ or mutein$ or variant$ or wild$)same (trimer$))	☐
S2025		USPT	(mutant$ or mutein$ or variant$ or wild$) same (trimer$)	☐
S2024		USPT	(mutant$ or mutein$ or variant$ or wild$) same (mutant$ or mutein$ or variant$ or wild$)	☐
S2023		USPT	dominant-negative or dominant adj negative	☐
S2022		USPT	trimer$	☐
S2021		USPT	mutant$ or mutein$ or variant$ or wild$	☐
S2020		USPT	trimer?	☐
			((wild or mutant$ or mutein$ or variant$ or (non-naturally adj	

S2019		USPT	occurring))and (tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor))and (trimer$)) and ((wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring))same (trimer$))	☐
S2018		USPT	((wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring))with (tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor))with (trimer$)) same (dominant-negative)	☐
S2017		USPT	(wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring)) same (trimer$)	☐
S2016		USPT	dominant-negative	☐
S2015		USPT	(wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring)) with (tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)) with (trimer$)	☐
S2014		USPT	(wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring)) and (tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)) and (trimer$)	☐
S2013		USPT	trimer$	☐

S2012		USPT	tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)	☐
S2011		USPT	wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring)	☐
S2010		USPT,PGPB,JPAB,EPAB,DWPI	(tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)) and (trim$) and (trimer$)	☐
S2009		USPT,PGPB,JPAB,EPAB,DWPI	trimer$	☐
S2008		USPT,PGPB,JPAB,EPAB,DWPI	trim$	☐
S2007		USPT,PGPB,JPAB,EPAB,DWPI	tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)	☐
S2006		USPT,PGPB,JPAB,EPAB,DWPI	wild or mutant$ or mutein$ or variant$ or (non-naturally adj occurring)	☐
S2005		USPT,PGPB,JPAB,EPAB,DWPI	((trimer$ or multimer$)with (mix$ or combination)) with (variant or mutant or mutein or (non-naturally adj occurring))	☐
S2004		USPT,PGPB,JPAB,EPAB,DWPI	((trimer$ or multimer$)with (mix$ or combination)) wit (variant or mutant or mutein or (non-naturally adj occurring))	☐
S2003		USPT,PGPB,JPAB,EPAB,DWPI	(trimer$ or multimer$) with (mix$ or combination)	☐
S2002		USPT,PGPB,JPAB,EPAB,DWPI	mix$ or combination	☐

S2001		USPT,PGPB,JPAB,EPAB,DWPI	((trimer$ or multimer$)with mix$) same (variant or mutant or mutein or (non-naturally adj occurring))	☐
S2000		USPT,PGPB,JPAB,EPAB,DWPI	((trimer$ or multimer$)with mix$) with (variant or mutant or mutein or (non-naturally adj occurring))	☐
S1999		USPT,PGPB,JPAB,EPAB,DWPI	variant or mutant or mutein or (non-naturally adj occurring)	☐
S1998		USPT,PGPB,JPAB,EPAB,DWPI	(trimer$ or multimer$) with mix$	☐
S1997		USPT,PGPB,JPAB,EPAB,DWPI	trimer$ or multimer$	☐
S1996		USPT,PGPB,JPAB,EPAB,DWPI	trimer$ or multimer$	☐
S1995		USPT	((variant or mutein or (non-naturally adj occurring))with (tNf or (tumor adj necrosis adj factor))) with trimer	☐
S1994		USPT	((variant or mutein)same trimer) with ((variant or mutein or (non-naturally adj occurring))with trimer)	☐
S1993		USPT	((variant or mutein or (non-naturally adj occurring))same (tNf or (tumor adj necrosis adj factor))) and trimer	☐
S1992		USPT	(variant or mutein or (non-naturally adj occurring)) same (tNf or (tumor adj necrosis adj factor))	☐

S1991		USPT	tNf or (tumor adj necrosis adj factor)	☐
S1990		USPT	(variant or mutein or (non-naturally adj occurring)) with trimer	☐

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